



MASSACHUSETTS

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Pharmacy Medical Policy Interleukin-2 (IL-2)

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Policy Number: 103

BCBSA Reference Number: None

Related Policies

None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Note: All requests for outpatient retail pharmacy for indications listed and not listed on the medical policy guidelines may be submitted to BCBSMA Clinical Pharmacy Operations by completing the Prior Authorization Form on the last page of this document.

We may cover **Proleukin®** (Aldesleukin) for adults (18 years and older) with a documented diagnosis of metastatic renal cell carcinoma.

We may cover **Proleukin®** (Aldesleukin) for adults (18 years and older) with a documented diagnosis of metastatic melanoma.

We may cover perilymphatic injection of IL-2 in patients with resectable, non-metastatic squamous cell cancer of the oral cavity and oropharynx.

We do not cover **Proleukin®** (Aldesleukin) for the treatment of other conditions not listed above because they are considered investigational.

We do not cover IL-2 in combination with chemotherapy or in combination with interferon alfa as a treatment of metastatic melanoma and renal cell cancer.

We do not cover IL-2 as a therapy to maintain remission after high-dose chemotherapy for a variety of malignancies, including multiple myeloma, leukemia, lymphoma, multiple myeloma, or breast cancer.

We do not cover other oncologic applications of IL-2 monotherapy, including but not limited to the following:

- Colorectal cancer

- Hepatocellular carcinoma
- Small-cell and non-small-cell lung cancers
- Acute leukemia
- Myelodysplastic syndromes
- Multiple myeloma
- Non-Hodgkin's and Hodgkin's lymphoma
- Ewing's sarcoma
- Soft tissue sarcoma
- Osteosarcoma
- Bladder
- Brain
- Breast
- Esophagus
- Ovary
- Pancreas
- Prostate
- Small bowel
- Stomach
- Testes, and
- Thyroid.

Other Information

Blue Cross Blue Shield of Massachusetts (BCBSMA*) members (other than Medex®; Blue MedicareRx, Medicare Advantage plans that include prescription drug coverage) will be required to fill their prescriptions for the above medications at one of the providers in our retail specialty pharmacy network, see link below:

[Link to Specialty Pharmacy List](#)

Individual Consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual’s unique clinical circumstances may be considered in light of current scientific literature. Physicians may send relevant clinical information for individual patients for consideration to:

Blue Cross Blue Shield of Massachusetts
 Pharmacy Operations Department
 25 Technology Place
 Hingham, MA 02043
 Tel: 1-800-366-7778
 Fax: 1-800-583-6289

Prior Authorization Information

Outpatient

For services described in this policy, see below for products where prior authorization **IS REQUIRED** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is required .
Commercial PPO and Indemnity	Prior authorization is required .

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member. Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria **MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:**

HCPCS Codes

HCPCS codes:	Code Description
J9015	Injection, aldesleukin, per single use vial (Proleukin, IL-2, Interleukin)

The following ICD Diagnosis Codes are considered medically necessary when submitted with the HCPCS code above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C04.9	Malignant neoplasm of floor of mouth, unspecified
C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C05.2	Malignant neoplasm of uvula
C05.8	Malignant neoplasm of overlapping sites of palate
C05.9	Malignant neoplasm of palate, unspecified
C06.0	Malignant neoplasm of cheek mucosa
C06.1	Malignant neoplasm of vestibule of mouth
C06.2	Malignant neoplasm of retromolar area
C06.80	Malignant neoplasm of overlapping sites of unspecified parts of mouth
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C06.9	Malignant neoplasm of mouth, unspecified
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C10.9	Malignant neoplasm of oropharynx, unspecified
C43.0	Malignant melanoma of lip
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal

C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C79.00	Secondary malignant neoplasm of unspecified kidney and renal pelvis
C79.01	Secondary malignant neoplasm of right kidney and renal pelvis
C79.02	Secondary malignant neoplasm of left kidney and renal pelvis
C79.2	Secondary malignant neoplasm of skin

Description

Interleukin-2 (IL-2) is a protein that occurs naturally in your body and plays an important role in activating your immune system. The immune system protects the body from foreign substances, cells, and tissues by responding to and resisting diseases. IL-2 activates specialized defense cells called T cells and natural killer (NK) cells to help attack and destroy invading germs or diseases. IL-2 can also stimulate these cells to attack and destroy cancerous tumors. PROLEUKIN® therapy is a genetically engineered or recombinant version of IL-2. PROLEUKIN® therapy helps activate the immune system to recognize and eliminate certain kinds of cancer cells.

Labeled indications for PROLEUKIN® (aldesleukin) approved by the U.S. Food and Drug Administration (FDA) include the treatment of metastatic renal cell carcinoma and metastatic malignant melanoma.

PROLEUKIN® therapy differs from other treatments for metastatic melanoma and metastatic kidney cancer because it's an immunotherapy. Instead of directly inhibiting cancer cells, it works to activate the body's immune system to help kill them.

Therapy with PROLEUKIN® (aldesleukin) for injection should be restricted to patients with normal cardiac and pulmonary functions as defined by thallium stress testing and formal pulmonary function testing. Extreme caution should be used in patients with a normal thallium stress test and a normal pulmonary function test who have a history of cardiac or pulmonary disease.

PROLEUKIN® should be administered in a hospital setting under the supervision of a qualified physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.

PROLEUKIN® administration has been associated with capillary leak syndrome (CLS) which is characterized by a loss of vascular tone, and extravasation of plasma proteins and fluid into the extravascular space. CLS results in hypotension and reduced organ perfusion which may be severe and can result in death. CLS may be associated with cardiac arrhythmias (supraventricular and ventricular),

angina, myocardial infarction, respiratory insufficiency requiring intubation, gastrointestinal bleeding or infarction, renal insufficiency, edema, and mental status changes.

PROLEUKIN® treatment is associated with impaired neutrophil function (reduced chemotaxis) and with an increased risk of disseminated infection, including sepsis and bacterial endocarditis. Consequently, preexisting bacterial infections should be adequately treated prior to initiation of PROLEUKIN® therapy. Patients with indwelling central lines are particularly at risk for infection with gram positive microorganisms. Antibiotic prophylaxis with oxacillin, nafcillin, ciprofloxacin, or vancomycin has been associated with a reduced incidence of staphylococcal infections.

Policy History

Date	Action
10/2018	Clarified coding information.
7/2018	Clarified coding information.
10/2017	Updated to change Walgreens Specialty Name.
7/2017	Updated to add AllCare to Pharmacy Specialty list.
6/2017	Updated address for Pharmacy Operations.
7/2015	Updated to add Walgreens Specialty.
7/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
2/2014	Updated Onco360 name and removed Curascript in Specialty Pharmacy section.
1/2014	Updated ExpressPath language.
4/2012	Updated specialty pharmacy contact information.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
6/1/2009	New policy, effective 6/1/2009, describing covered and non-covered indications.

References

1. Proleukin [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2007.
2. Yang JC, Sherry RM, Steinberg SM et al. Randomized study of high-dose and low-dose interleukin-2 in patients with metastatic renal cell cancer. *J Clin Oncol* 2003; 21(16):3127-32.
3. Clark JI, Atkins MB, Urba WJ et al. Adjuvant high-dose bolus interleukin-2 for patients with high-risk renal cell carcinoma: a cytokine working group randomized trial. *J Clin Oncol* 2003; 21(16):3133-40.
4. Negrier S, Caty A, Lesimple T et al. Treatment of patients with metastatic renal carcinoma with a combination of subcutaneous interleukin-2 and interferon alfa with or without fluorouracil. *J Clin Oncol* 2000; 18(24):4009-15.
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6. Henriksson R, Nilsson S, Colleen S et al. Survival in renal cell carcinoma - a randomized evaluation of tamoxifen vs. interleukin 2, alpha interferon and tamoxifen. *Br J Cancer* 1998; 77(8):1311-7.
7. Rosenberg SA, Yang JC, Schwartzentruber DJ et al. Prospective randomized trial of the treatment of patients with metastatic melanoma using chemotherapy with cisplatin, dacarbazine, and tamoxifen alone or in combination with interleukin-2 and interferon alfa-2b. *J Clin Oncol* 1999; 17(3):968-75.
8. Ridolfi R, Chiarion-Sileni V, Guida M et al. Cisplatin, dacarbazine with or without subcutaneous interleukin-2 and interferon alfa-2b in advanced melanoma outpatients: results from an Italian Multicenter Phase III randomized clinical trial. *J Clin Oncol* 2002; 20(6):1600-7.
9. Eton O, Legha SS, Bedikian AY et al. Sequential biochemotherapy versus chemotherapy for metastatic melanoma: results from a phase III randomized trial. *J Clin Oncol* 2002; 20(8):2045-52.
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11. Atzpodien J, Neuber K, Kamanabrou D et al. Combination chemotherapy with or without s.c. IL-2 and IFN-alpha: results of a prospectively randomized trial of the Cooperative Advanced Malignant Melanoma Chemoimmunotherapy Group (ACIMM). *Br J Cancer* 2002; 86(2):179-84.

12. Attal M, Blaise D, Marit G et al. Consolidation treatment of adult acute lymphoblastic leukemia: a prospective, randomized trial comparing allogeneic versus autologous bone marrow transplantation and testing the impact of recombinant interleukin-2 after autologous bone marrow transplantation. *Blood* 1995; 86(4):1619-28.
13. Klingeman HG, Phillips GL. Is there a place for immunotherapy with interleukin-2 to prevent relapse after autologous stem cell transplantation for acute leukemia? *Leuk Lymphoma* 1995; 16(5-6):397-405.
14. Blaise D, Attal M, Pico JL et al. The use of a sequential high dose recombinant interleukin 2 regimen after autologous bone marrow transplantation does not improve the disease free survival of patients with acute leukemia transplanted in first complete remission. *Leuk Lymphoma* 1997; 25(5-6):469-78.
15. Nagler A, Ackerstein A, Or R et al. Immunotherapy with recombinant interleukin-2 and recombinant interferon-alpha in lymphoma patients postautologous bone marrow or stem cell transplantation. *Blood* 1997; 89(11):3951-9.
16. Cortes JE, Kantarjian HM, O'Brien S et al. A pilot study of interleukin-2 for adult patients with acute myelogenous leukemia in first complete remission. *Cancer* 1999; 85(7):1506-13.
17. De Stefani A, Forni G, Ragona R et al. Improved survival with perilymphatic interleukin 2 in patients with resectable squamous cell carcinoma of the oral cavity and oropharynx. *Cancer* 2002; 95(1):90-7.
18. www.cancer.gov/search/clinical_trial

To request prior authorization using the Massachusetts Standard Form for Medication Prior Authorization Requests (eForm), click the link below:

<http://www.bluecrossma.org/medical-policies/sites/g/files/csphws2091/files/acquiadam-assets/023%20E%20Form%20medication%20prior%20auth%20instruction%20prn.pdf>



Home Infusion Therapy Prior Authorization Form

Please complete and fax with the physician's prescription to: (888) 641-5355. If the patient is a BCBSMA employee, please fax the form to: (617)246-4013. If the patient is a Blue MedicareRx member, please fax the request to Anthem Blue Cross Blue Shield at (866) 827-9822.

FOR TPN THERAPY, USE MEDICAL POLICY #296 REQUEST FORM

Company name:		Contact Name:	
Phone #:		Provider #:	
Fax#		Address:	
Patient name:		Address:	
Patient ID#:		DOB: ___/___/___	Diagnosis:
Prescribing Physician/addr:	_____	Telephone:	_____
PCP name/address:	_____	Telephone:	_____

Is this fax number 'secure' for PHI receipt/transmission per HIPAA requirements? (circle one) Yes No
 Place of Service Home SNF MD office other (specify)

Primary Therapy

Primary drug name: _____ Approximate duration: ___/___/___ to ___/___/___
 Dose: _____
 Frequency: _____ Route of Administration: _____ pump: Y___ N___

Other Therapy

Other drug name: _____ Approximate duration: ___/___/___ to ___/___/___
 Dose: _____
 Frequency: _____ Route of Administration: _____ pump: Y___ N___

If this is a "drug only" authorization request, indicate other services the nursing agency is providing:

Nursing provided by: _____ Contact: _____
 Phone: _____
 Fax: _____

Request for 7 Day Coverage: Date of occurrence: _____ Request dates: _____
 Occurrence type: Hospitalization Death Change of Therapy

Physician signature: _____
 Date: _____

OR Copy of prescription REQUIRED with this request.